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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/227,854	01/11/1999	JIAN NI	PF210D1	7606

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EXAMINER	
PRASAD, SARADA C	
ART UNIT	**PAPER NUMBER**
1646	15

DATE MAILED: 01/29/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Applicati n No. 09/227,854	Applicant(s) NI ET AL.	
	Examiner Sarada C Prasad	Art Unit 1646	

-- The MAILING DATE of this communication appears on th cover sheet with the c rrespondence address --

Peri d for R ply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 November 2001* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *35-54 and 60-70* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *35-54 and 60-70* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *13* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

Detailed Action

1. Receipt of Applicants' arguments and amendments filed in Paper No. 14 (11/15/01) is acknowledged. Claims 1-19, 25-34, and 5-59 have been cancelled; new claims 60-70 have been added. Currently, claims 35-54, and 60-70 are under consideration.

2. Based on Applicants' arguments, the following rejections are withdrawn:

(i) rejection of claims 35-54, and 60-70 under 35 USC § 101 based on utility.

3. Applicants' arguments filed in Paper No. 14 (11/15/01), have been fully considered but were deemed persuasive in part. The issues remaining and new issues, are stated below. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Specification

4. Figure 3 is objected to because the brief description on page 7 of the specification for Figure 3 states that it is directed to 'show the structural and functional features of the polypeptide ...' while Figure 3, in fact, is a western blot. Appropriate correction is required.

Claim Rejections - 35 USC § 112-First paragraph

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5a. Claims 35-54, 60-70 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated polypeptide of SEQ ID NO. 2, does not reasonably provide enablement for the claimed protein variants that comprise 30 or 50 contiguous amino acid residues of SEQ ID NO. 2, or 30 or 50 contiguous amino acid residues of

a polypeptide encoded by the human cDNA contained in ATCC Deposit No. 97304 or an isolated polypeptide comprising a first amino acid sequence 90%, or more identical to a second amino acid sequence selected from the group consisting of amino acid residues 2-92 of SEQ ID No. 2, or amino acids 1-92 of SEQ ID No. 2, or amino acid sequence of the mature polypeptide encoded by the cDNA in ATCC Deposit No. 97304, or aminoacid sequence of the full length polypeptide encoded by the cDNA in ATCC Deposit No. 97304. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

The factors to be considered have been summarized as the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples, the nature of the invention, the state of the prior art and the breadth of the claims. Ex Parte Forman (230 USPQ 546(Bd Pat. App. & Int. 1986)); In re Wands, 858 F.2d 1400 (Fed. Cir. 1988).

Applicants cite post-filing date reference of Miranda et al. disclosing that the human S100A12 mediates the chemotaxis of neutrophils and macrophages (Page 7, 1st para), and suggest that the instant SEQ ID NO. 2, identical to the S100A12, plays a role in the recruitment of leukocyte sub-populations (page 9, 2nd para of Paper No. 14). Because the polypeptide disclosed by Miranda et al. is identical to the CCI amino acid sequence of SEQ ID No. 2, Applicants claim that their assertion of a specific utility i.e., that mediation of recruitment of leukocytes by the CCI protein is a confirmed feature, and the hence the specification is enabling for use of the instant SEQ ID No. 2, wherever recruitment of leukocytes is needed, such as enhancement of host defenses against resistant chronic and acute infections, for example

mycobacterial infections via the attraction and activation of microbial leukocytes (page 21, lines 31-34 of specification).

Based on the post-filing date publication of Miranda et al. the 35 USC § 101 based utility is withdrawn. However, while persuasive with respect to 35 USC 101, Applicants' arguments are not found persuasive with respect to 35 USC 112-first paragraph because, Miranda et al. disclose only attraction and not activation of neutrophils and macrophages, and this feature of S100A12 has not been indicated to be generic to include leukocytes as well. Assuming for the sake of argument that the Applicants have extrapolated the potential of the instant CCI to attract and activate leukocytes as well, the specification fails to disclose as to how to use the protein to treat acute, or resistant chronic infections.

Applicants assert that the initial burden is on the Examiner to establish why one of ordinary skill in the art would reasonably doubt Applicants' assertion of utility and as a consequence, enablement (page 6, 2nd para, lines 1-2 of paper No. 14). Examiner's position for maintaining the instant lack of enablement rejection is as follows:

The rejection based on enablement, directed also to claims 35-54 and 60-70, is maintained because the disclosure fails to provide guidance of how to use the variant polypeptides generated while citing general features, without specific details such as (i) what are the 30 or 50 contiguous amino acids to select from in generating polypeptides as recited in claims 35-41, or what are the permitted amino acid changes to obtain a first amino acid with 90% or more identical to a second amino acid sequence selected from the either the polypeptide of SEQ ID No. 2 or from a polypeptide encoded by the cDNA of the ATCC Deposit No. 97304. At the time the invention was made (provisional application with ser no. 60/008,387-FD 12/8/97 or

parent application 08/761,289-FD 12/6/96), it is only the sequence of CCI that was disclosed, and not the success of its contemplated utility. Even, five years later, Miranda et al. (12/20/2001) showed only its chemotactic activity to neutrophils and macrophages in vitro and not has been extrapolated to include leukocytes. Therefore, one of skill in the art would reasonably conclude that the applicants failed to provide guidance as to how to use the instant polypepide, nor were enabled for the claimed use of the instant CCI polypeptide for treatment of acute and chronic infections. It would be undue experimentation for one of skill in the art to make these undescribed variants of SEQ ID No. 2 that would be functionally equivalent to what is expected of the instant CCI, which is similar to the S100A2 protein of Miranda et al.

The test of enablement is not whether any experimentation is necessary, but whether, if experimentation is necessary, it is undue. Based on the above discussion, due to lack of sufficient guidance as to how to use the instant CCI for treatment of acute or chronic infections, and predictability in the art that would require establishment of specificity of the instant SEQ ID NO. 2 to be effective on leukocytes, the specification is non-enabling for the practice of instant claims and the rejection of record is being maintained.

5b. Claims 42, and 60(c) are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention as in Paper No. 10 (6/15/01).

This rejection of record is being maintained because the Applicants did not have possession of the mature polypeptide as recited in claims 42 and 60(c).

Applicants assert that none of the pending claims recite secreted forms of the polypeptides and only claims 42 and 60(c) recite the mature polypeptide encoded by the cDNA in ATCC Deposit No. 97304 (page 13 of Paper No. 14); by disclosing the plasmid that inherently encodes the mature form of the protein, the specification necessarily discloses the mature protein generated by the expression of the plasmid; as such the disclosure of the complete amino acid sequence of CCI in the specification at Figures 1 and 2, and SEQ ID No. 2, combined with the deposited plasmid, is sufficient to enable one of skill in the art to make and/or use the claimed invention (page 14, entire 1st para). It is true that only claims 42 and 60 (c) recite the mature polypeptide, and the instant rejection based on mature polypeptide is directed to these claims. Applicants' arguments and assertions of having possession of mature polypeptide of SEQ ID No. 2 are fully considered, however, not found to be persuasive, because generation of mature polypeptide depends on host cell and often a single organism will make more than one "mature form" at different developmental stages or in different tissues. The structure of the "mature" protein is therefore not inherent to the nucleic acid that encodes it. Therefore, based on the disclosure, and applicants' arguments, one of skill in the art would realize that the Applicants are not in possession of the mature polypeptide of instant SEQ ID NO. 2 at the time of filing, and the claims are directed to 'contemplated or wish to know' aspect of the mature polypeptide of instant SEQ ID No. 2.

It is believed that all of Applicants' arguments have been addressed and based on the above discussion, the instant rejection of claims 42, 60(c) is maintained.

Claim Rejections - 35 USC § 102

6. Claims 35-59 remain rejected under 35 U.S.C. 102(e) as being anticipated by Hitomi et al. This rejection of record is being maintained for reasons of record set forth in the previous office action (Paper No. 10, 6/15/01) as well as additional reasons listed as follows.

Response to declaration under 37 C.F.R. 1.131:

The declaration filed on 4/21/2001 under 37 CFR 1.131 has been considered but is ineffective to overcome the Hitomi et al. reference.

The evidence submitted is insufficient to establish a conception of the invention prior to the effective date of the Hitomi et al. reference. While conception is the mental part of the inventive act, it must be capable of proof, such as by demonstrative evidence or by a complete disclosure to another. Conception is more than a vague idea of how to solve a problem. The requisite means themselves and their interaction must also be comprehended. See *Mergenthaler v. Scudder*, 1897 C.D. 724, 81 O.G. 1417 (D.C. Cir. 1897).

In this case, there is not even a vague idea of a problem to be solved. Under 37CFR 1.131, applicant may show any of the following to antedate a reference:

A) reduction to practice prior to the effective date of the reference;

B) conception prior to the effective date of the reference coupled with subsequent due delegence to reduce to practice, or

C) conception of the invention prior to the effective date of the reference coupled with due delegence from prior to the reference date to the filing date of the application. See MPEP 715.07.

In the instant case, the declaration under 1.131 shows only a nucleic acid sequence. While such sequence is necessary to disclose conception of the invention, it is not sufficient. There are no facts or evidence to show that the inventors knew what the sequence was, i.e., any protein encoded thereby, or any concept of what the nucleic acid, or encoded protein would be used for, or any function associated with such. In the absence of any such information, the mere existence of the sequence is not sufficient to establish conception of the invention prior to the effective date of the reference. Therefore, the outstanding 102(e) rejection of record for claims 35-59 is being maintained.

Conclusion

7. No claims are allowable.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sarada C Prasad whose telephone number is 703-305-1009. The examiner can normally be reached Monday – Friday from 8.00 AM to 4.30 PM (Eastern time).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler, can be reached on (703) 308-6564. The fax phone number for the organization where this application or proceeding is assigned is 703-308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Sarada Prasad, Ph.D.
Examiner
Art Unit 1646
January 25, 2002

LORRAINE SPECTOR
PRIMARY EXAMINER